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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/045,204	10/24/2001	Grigori N. Enikolopov	1314.1044-017	3409

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NEW YORK, NY 10020-1105

EXAMINER

CRIARES, THEODORE J

ART UNIT	PAPER NUMBER
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1617

DATE MAILED: 09/16/2003

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/045,204

Applicant(s)

ENIKOLOPOV ET AL.

Examiner

Theodore J. Criares

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 25 June 2003.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 20-22 and 43-47 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 20-22 and 43-47 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- ☐ Notice of References Cited (PTO-892)
- ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
- ☐ Interview Summary (PTO-413) Paper No(s). _____.
- ☐ Notice of Informal Patent Application (PTO-152)
- ☐ Other:

CLAIMS 20-22 AND 43-47 ARE PRESENTED FOR

EXAMINATION

DETAILED ACTION

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 20-22 and 43-47 are rejected under 35 U.S.C. 112, first paragraph, because the specification is not enabled for a method of increasing a population of dividing cells in a tissue of a mammal, comprising contacting said tissue with an inhibitor of nitric oxide (NO) or nitric oxide synthase (NOS), thereby increasing dividing cells in the tissue. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

Enablement is considered in view of the Wands factors (MPEP 2164.01(a)).

These include: nature of the invention, breadth of the claims, guidance of the specification, the existence of working examples, predictability of the prior art, state of the prior art and the amount of experimentation necessary. All of the **Wands factors** have been considered with regard to the instant claims, with the most relevant factors discussed below.

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Nature of the Invention: All of the rejected claims are drawn to a method of increasing dividing cell in a tissue of a mammal. The nature of the invention is extremely complex in that it encompasses the actual increase in embryonic dividing cells and requires a full teaching and exemplification to consider it enabled. There is a lack of teaching in the specification of dosage required to increase the dividing cells of claims 2-22 and 43-47 and the NO or NOS required to increase the dividing cell in each of the tissues of claims 43-47.

Breath of the Claims: The complex of nature of the subject matter being claimed are greatly exacerbated by breath of the claims. The claims encompass any amount of nitric oxide inhibitor and any one of the known NOI agents to be administered to increase dividing cells in tissue.

Guidance of the Specification: The guidance given by the specification as to how one would administer the claimed compounds to a subject in order to actually increase the dividing cells is minimal. All of the guidance provided by the specification is directed towards the increase of hemopoietic and bone cells. The dosage of NO or NOS to be used to treat a specific tissue is not taught by the specification. The only guidance is a broad allegation at page 22, line 17 to page 23, line 2 that a broad range of dosages can be used of from 1 mg/kg to 1000 mg/kg of body weight can be used. There is a lack of nexus between the NO and NOS compounds which can be used to the tissue in which the dividing cells are to be increased.

There is also a lack of teaching in the specification which of the compounds listed at page 8, line 3 to page 9, line 10 can be administered to cause an increase in a specific tissue.

Working Examples: All of the working examples provided by the specification are directed toward the BrdU-labeled cells and hematopoiesis. There is no nexus which shows the ability of NO to increase dividing cells in tissues as claimed by applicants in claims 43-47.

State of the Art: While there is literature as set forth in the specification at page 1, line 15 to page 2 line 12 where it is acknowledged that little is known about the signals that cause discrete groups of cells and organs to terminate growth at the appropriate cell number and size. In particular, there does not appear to be any examples or teachings in the prior art wherein a compound similar to the claimed compounds was administered to a subject to control growth of cells in tissues, e.g., skin tissue, epithelial tissue, tendon tissue, etc.

Predictability of the Art: The lack of significant guidance from the specification or prior art with regard to the actual amounts to be utilized and use of similar compounds to control the development of dividing cells in a human subject with the claimed compounds makes practicing the claimed invention unpredictable.

The amount of Experimentation Necessary: In order to practice claimed invention, one of skilled in the art would have to first envision the compound, dosage of compound to be used, the tissue for which it is suitable and appropriate animal model system for one of the claimed compounds and test the

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combination in the model system to determine whether or not the combination is effective for increasing dividing cells in tissues.. If unsuccessful, which is likely given the lack of significant guidance from the specification or prior art, one of skill in the art would have to then either envision a modification of the first combination of pharmaceutical compound, compound dosage, animal model system, or envision an entirely new combination of the above, and test the system again. If again unsuccessful, which is likely given the lack of significant guidance from the specification or prior art regarding cell proliferation, the entire, unpredictable process would have to be repeated until successful. Therefore, it would require undue, unpredictable experimentation to practice the claimed invention to increase dividing cells in tissue.

Therefore, a method of increasing a dividing cells in a tissue of a mammal, comprising contacting dividing cell with a nitric oxide inhibitor oxide, thereby obtaining an increase in dividing cells is not considered to be enabled by the instant specification.

None of the claims are allowed.


Any inquiry concerning this communication or earlier communications from the examiner should be directed to Theodore J. Criares whose telephone number is 308-4607. The examiner can normally be reached on 6:30 A.M. to 5:00P.M. Monday through Thursday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreenivasan Padmanabhan can be reached on 305-1877. The fax phone

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number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 308-1235.



Theodore J. Criares
Primary Examiner
Art Unit 1617

TJC
September 15, 2003